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Customer No.: 32801

Docket No: 0630/1E791-US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Vedrana S. SUSULIC; Emir DUZIC

Serial No.: 09/761,116 Art Unit: 1636

Confirmation No.: 3094

Filed: January 16, 2001 Examiner: Leffers Jr., Gerald

For: TRANSCRIPTIONAL REGULATION OF THE HUMAN BETA3 - ADRENERGIC RECEPTOR GENE

COURTESY COPY OF CLAIMS PENDING UPON ENTRY OF ACCOMPANYING AMENDMENT

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

April 14, 2003

Sir:

28. (Twice Amended) A method of screening for a compound that increases activity of an Sp1 or B segment-binding β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the Sp1 or B segment-binding β_3-AR *trans*-activating factor with a test compound; and

(b) detecting an increase in a level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor,

wherein the increase in the level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor results in an increase in the level of β_3-AR gene product relative to a level of expression prior to contact with the test compound.

29. (Allowed) A method of screening for a compound that increases activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting an increase in a level of activity of the β_3-AR *trans*-activating factor, wherein the increase in the level of activity of

the β_3-AR *trans*-activating factor is detected by detecting an increase in the level of expression of a reporter gene operatively associated with an isolated nucleic acid having a nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) relative to a level of expression prior to contact with the test compound.

30. (Amended) A method according to claim 28, wherein the increase in the level of activity of the β_3-AR *trans*-activating factor is detected by detecting an increase in the amount of β_3-AR *trans*-activating factor present in the cells after contacting them with the test compound relative to the amount present prior to contact with the test compound.

31. A method according to claim 28, wherein the cells do not endogenously express, or express at very low level, β_3-AR.

32. A method according to claim 31, wherein the cells are selected from the group consisting of HeLa cells, CV-1cells, and WAT cells.

33. (Twice Amended) A method of screening for a compound that inhibits activity of an Sp1 or B segment-binding β_3-adrenergic receptor (β_3-AR)

trans-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the Sp1 or B segment-binding β_3-AR *trans*-activating factor with a test compound; and

(b) detecting a decrease in a level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor,

wherein the decrease in the level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor results in a decrease in the level of β_3-AR gene product relative to a level of expression prior to contact with the test compound.

34. (Allowed) A method of screening for a compound that inhibits activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting a decrease in a level of activity of the β_3-AR *trans*-activating factor,

wherein the decrease in the level of activity of the β_3-AR *trans*-activating factor is detected by detecting a decrease in the level of expression of a reporter gene operatively associated with an isolated nucleic acid having a nucleotide sequence

GCCTCTGGGGAG (SEQ ID NO:1) relative to a level of expression prior to contact with the test compound.

35. A method according to claim 33, wherein the decrease in the level of activity of the β_3-AR trans-activating factor is detected by detecting a decrease in the amount of β_3-AR trans-activating factor present in the cells after contacting them with the test compound relative to the amount present prior to contact with the test compound.

36. A method according to claim 33, wherein the cells endogenously express β_3-AR.

37. A method according to claim 36, wherein the cells are selected from the group consisting of neuroblastoma and BAT cells.

38. (Amended) A method of screening for a compound that increases activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting an increase in a level of activity of the β_3-AR *trans*-activating factor,

wherein the level of activity of the β_3-AR *trans*-activating factor is detected by an increase in the level of expression of a reporter gene operatively associated with an isolated nucleic acid selected from the group consisting of:

(i) about a 7 kb genomic DNA 5' flanking region of a β_3-AR transcription start site,

(ii) a deletion construct of a 7 kb genomic DNA located upstream of a β_3-AR transcription start site;

(iii) a nucleic acid comprising a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) located 5' to an Sp-1 binding site relative to a transcription start site; and

(iv) a nucleic acid comprising a heterologous coding sequence operatively associated with a promoter and operatively associated with a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) in proximity to an Sp-1 binding site, whereby expression of the heterologous protein is regulated in a tissue specific manner.

39. (Amended) A method of screening for a compound that decreases activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in

human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting a decrease in a level of activity of the β_3-AR *trans*-activating factor, wherein the level of activity of the β_3-AR *trans*-activating factor is detected by a decrease in the level of expression of a reporter gene operatively associated with an isolated nucleic acid selected from the group consisting of:

(i) about a 7 kb genomic DNA 5' flanking region of a β_3-AR transcription start site,

(ii) a deletion construct of a 7 kb genomic DNA located upstream of a β_3-AR transcription start site;

(iii) a nucleic acid comprising a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) located 5' to an Sp-1 binding site relative to a transcription start site; and

(iv) a nucleic acid comprising a heterologous coding sequence operatively associated with a promoter and operatively associated with a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) in proximity to an Sp-1 binding site, whereby expression of the heterologous protein is regulated in a tissue specific manner.

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